

FIGURE 1

mAb	Mean Fluorescence Intensity		% Gated	
	L1.2-CCR5	PBMC	L1.2-CCR5	PBMC
mouse IgG1	10	4	1	1
2D7	75	29	92	36
PA8	48	9	73	3
PA9	79	5	96	3
PA10	80	8	96	5
PA11	107	8	96	10
PA12	115	8	96	8
PA14	81	14	96	22

#4

FIGURE 2

INHIBITOR COMBINATION	CONCENTRATION RATIO	ASSAY	COMBINATION INDEX	
			90% Inhibition	50% Inhibition
PA12:2D7	10:1	Entry	0.043	0.291
	2:1	Fusion	0.017	0.019
	10:1	Fusion	0.087	0.067
	50:1	Fusion	0.158	0.046
PA12:PA14	10:1	Entry	0.437	0.535
	10:1	Fusion	0.22	0.263
PA14:2D7	1:1	Entry	2.85	1.85
	1:1	Fusion	1.34	1.74
PA12:PA11	1:1	Entry	0.707	0.641
PA12:RANTES	1000:1	Fusion	0.331	0.156
PA14:RANTES	100:1	Fusion	1.6	1.37
2D7:RANTES	100:1	Fusion	0.972	0.962
PA12:CD4-IgG2	10:1	Fusion	0.3	0.31
PA14:CD4-IgG2	1:1	Fusion	0.957	0.566
2D7:CD4-IgG2	1:1	Fusion	1.127	0.302

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FIGURE 3

	Epitopes	IC <sub>50</sub> values (µg/ml)			
		cell-cell fusion inhibition	viral entry inhibition	gp120-binding inhibition	calcium flux inhibition
PA8	Nt	-	-	-	-
PA9	Nt/ECL2	-	-	0.24	-
PA10	Nt/ECL2	-	-	0.13	-
PA11	Nt	25.5	-	0.33	-
PA12	Nt	10.0	-	0.24	-
PA14	Nt/ECL2	1.7	.024	1.58	6.4
2D7	ECL2	1.6	.026	1.38	45

FIGURE 4

		1		5		10		15		20		25		30																		
		M	D	Y	Q	V	S	S	P	I	Y	D	I	N	Y	Y	T	S	E	P	C	Q	K	I	N	K	Q	I	A	A	A	R
Nt	2D7	X	92	54	90	nd	83	63	82	nd	46	40	X	40	90	90	86	111	49	37	45	44	37	X	32	27	92	X	X	X	X	65
	PA8	X	118	63	78	nd	52	36	32	nd	4	-2	X	-33	-7	45	100	47	32	36	44	37	X	34	-24	134	X	X	X	X	36	
	PA9	X	-16	-13	0	nd	213	-10	-13	nd	10	0	X	-19	-62	32	29	71	36	32	36	45	30	X	55	-18	145	X	X	X	40	
	PA10	X	-21	-14	0	nd	173	39	-22	nd	14	8	X	-15	-101	48	49	94	27	47	45	45	39	X	53	-13	133	X	X	X	46	
	PA11	X	31	70	32	0	nd	112	80	81	nd	40	-22	X	51	74	70	46	85	32	47	36	48	40	X	47	-22	144	X	X	84	
	PA12	X	68	30	0	nd	76	81	51	nd	34	-12	X	49	76	68	40	86	30	41	49	46	34	X	54	-12	93	X	X	43		
	PA14	X	5	86	75	nd	85	88	89	nd	57	40	X	64	78	84	66	76	80	71	44	86	64	X	76	46	99	X	X	33		
		90		95		100																										
		H	Y	A	A	A	Q	W	D	F	G	N	T	M	C	Q																
ECL1	2D7	70	89	X	X	X	40	138	40	66	X	58	72	82	0	74																
	PA8	38	92	X	X	X	49	118	32	113	X	96	86	68	-10	39																
	PA9	31	66	X	X	X	27	81	-16	139	X	138	89	57	0	43																
	PA10	67	83	X	X	X	36	139	-18	133	X	113	97	61	0	40																
	PA11	39	81	X	X	X	38	91	-23	78	X	60	94	71	-10	60																
	PA12	63	67	X	X	X	35	91	29	77	X	76	79	102	-25	55																
	PA14	73	79	X	X	X	63	83	-23	86	X	47	89	80	0	77																
		170		175		180		185		190																						
		R	S	Q	K	E	G	L	H	Y	T	C	S	S	H	F	P	Y	S	Q	Y	Q	F	W	K	N	F	Q				
ECL2	2D7	62	55	17	0	X	X	X	62	64	65	0	83	95	33	32	32	80	92	73	92	34	73	39	33	45	103					
	PA8	38	40	58	31	X	X	X	65	93	83	26	90	100	31	51	46	90	69	74	59	38	95	33	40	27	62					
	PA9	39	38	63	15	X	X	X	34	73	0	79	93	112	27	43	77	79	63	75	74	-10	31	38	-12	35	39					
	PA10	45	59	34	-19	X	X	X	30	-21	0	23	84	96	37	61	19	77	82	53	68	-6	39	95	-16	38	70					
	PA11	67	58	45	33	X	X	X	49	138	130	17	78	95	40	48	38	91	99	81	34	-14	73	47	-23	50	92					
	PA12	32	56	36	31	X	X	X	32	102	134	39	73	85	44	49	42	101	90	45	34	-23	66	37	28	33	74					
	PA14	-1	85	88	39	X	X	X	80	-20	72	9	109	83	52	64	50	40	93	88	63	34	79	35	51	72	71					
		265		270		275																										
		Q	E	F	F	G	L	N	N	C	S	S	S	N	R	L	D	Q														
ECL3	2D7	X	83	35	29	X	X	X	77	61	60	71	71	78	68	77	X	136														
	PA8	X	78	-25	0	X	X	X	37	43	42	85	71	73	86	99	X	98														
	PA9	X	32	-22	-1	X	X	X	67	40	50	71	81	77	90	93	X	112														
	PA10	X	41	-25	-4	X	X	X	64	60	56	93	103	49	74	72	X	128														
	PA11	X	60	38	-10	X	X	X	35	60	49	78	72	70	72	75	X	166														
	PA12	X	60	28	-11	X	X	X	34	36	46	83	72	99	82	78	X	131														
	PA14	X	92	82	42	X	X	X	80	31	92	108	90	98	74	78	X	112														

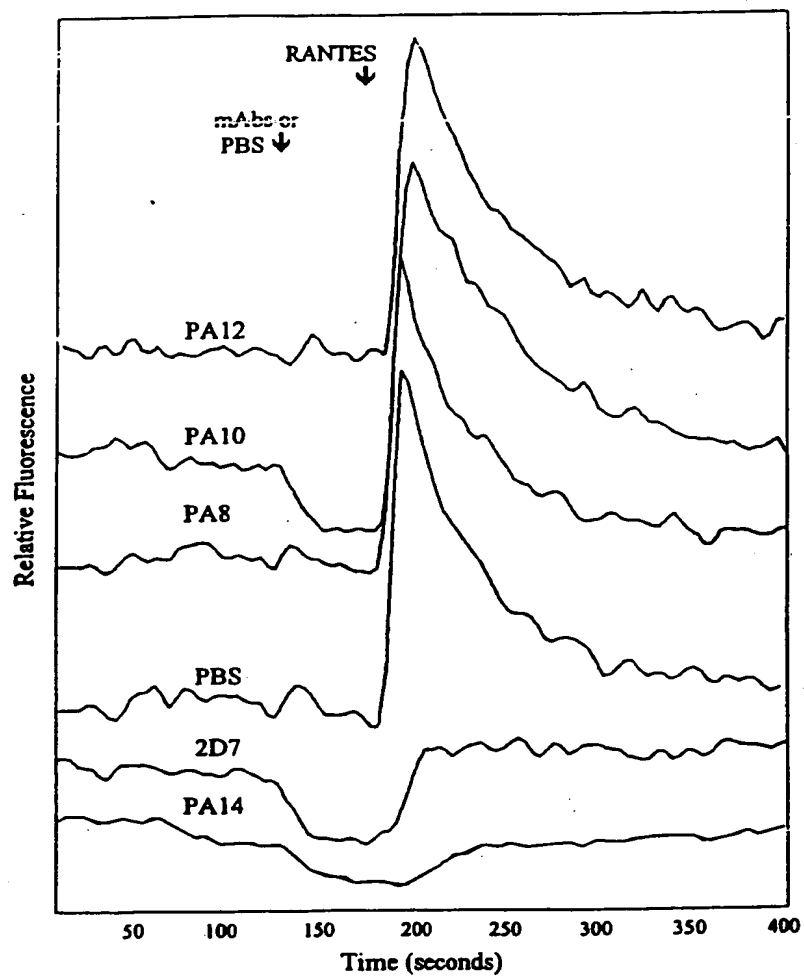
76%-100%  
51%-75%  
26%-50%  
0%-25%  
nd

76%-100+%  
 51%-75%  
 26%-50%  
 0%-25%  
 nd



5/20

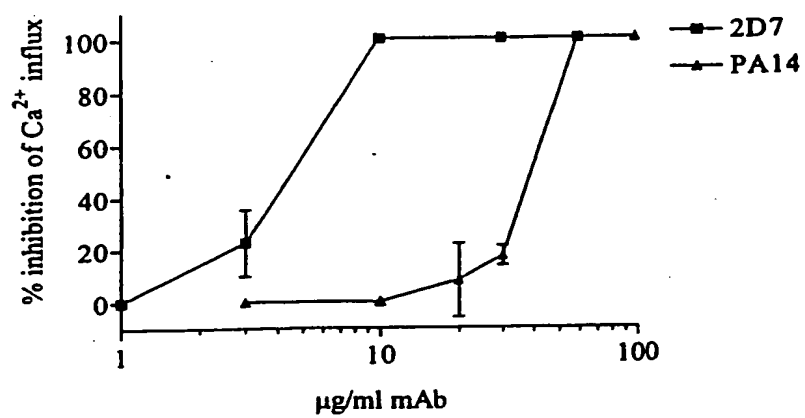
FIGURE 5A



00828615-031601  
109180-51982800

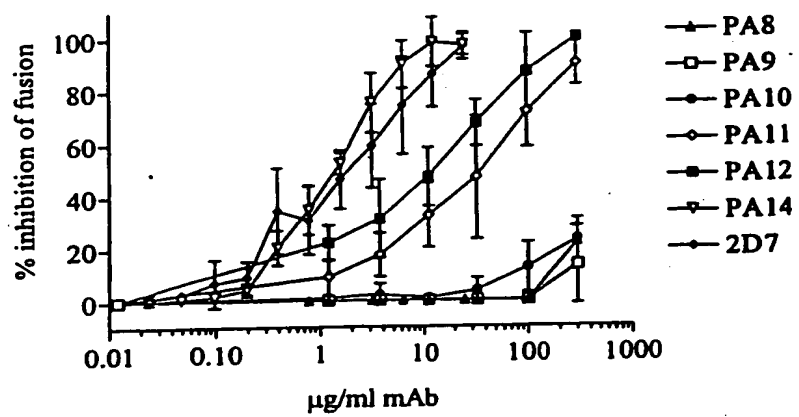
6/20

FIGURE 5B



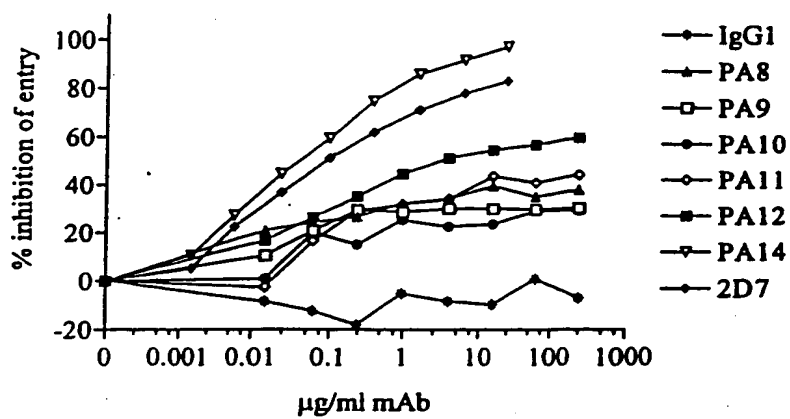
7/20

FIGURE 6A



8/20

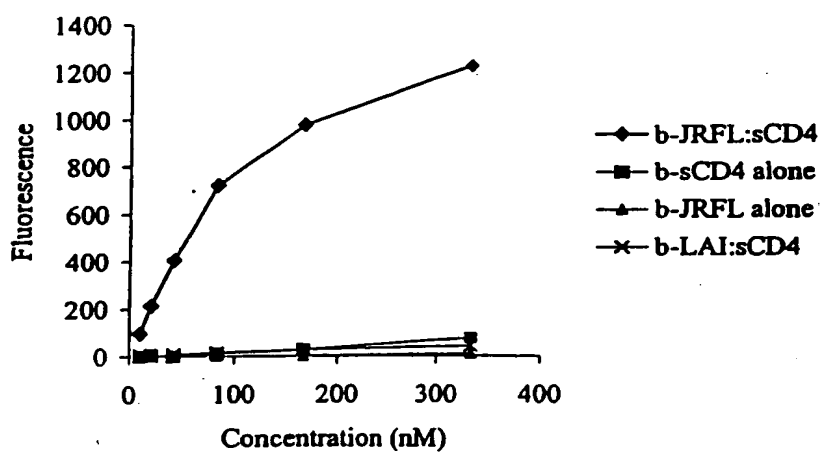
FIGURE 6B





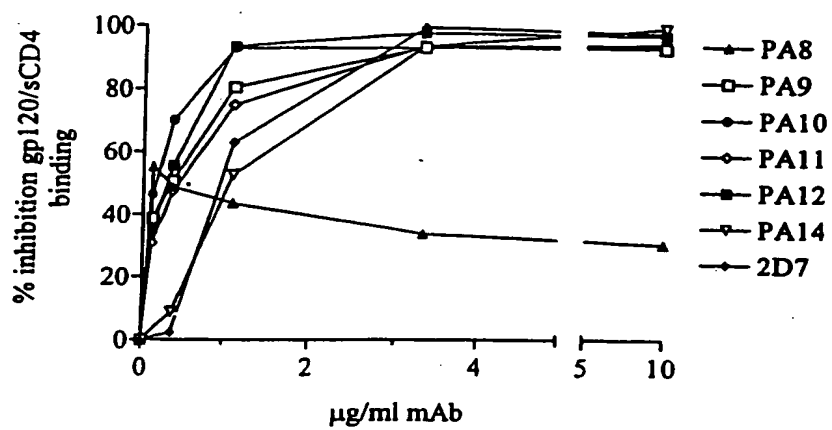
9/20

FIGURE 6C



10/20

FIGURE 6D



11/20

FIGURE 7

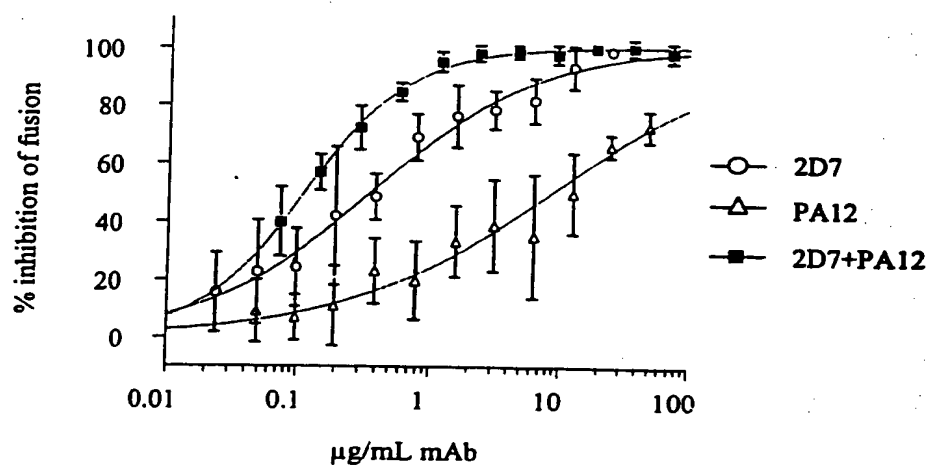
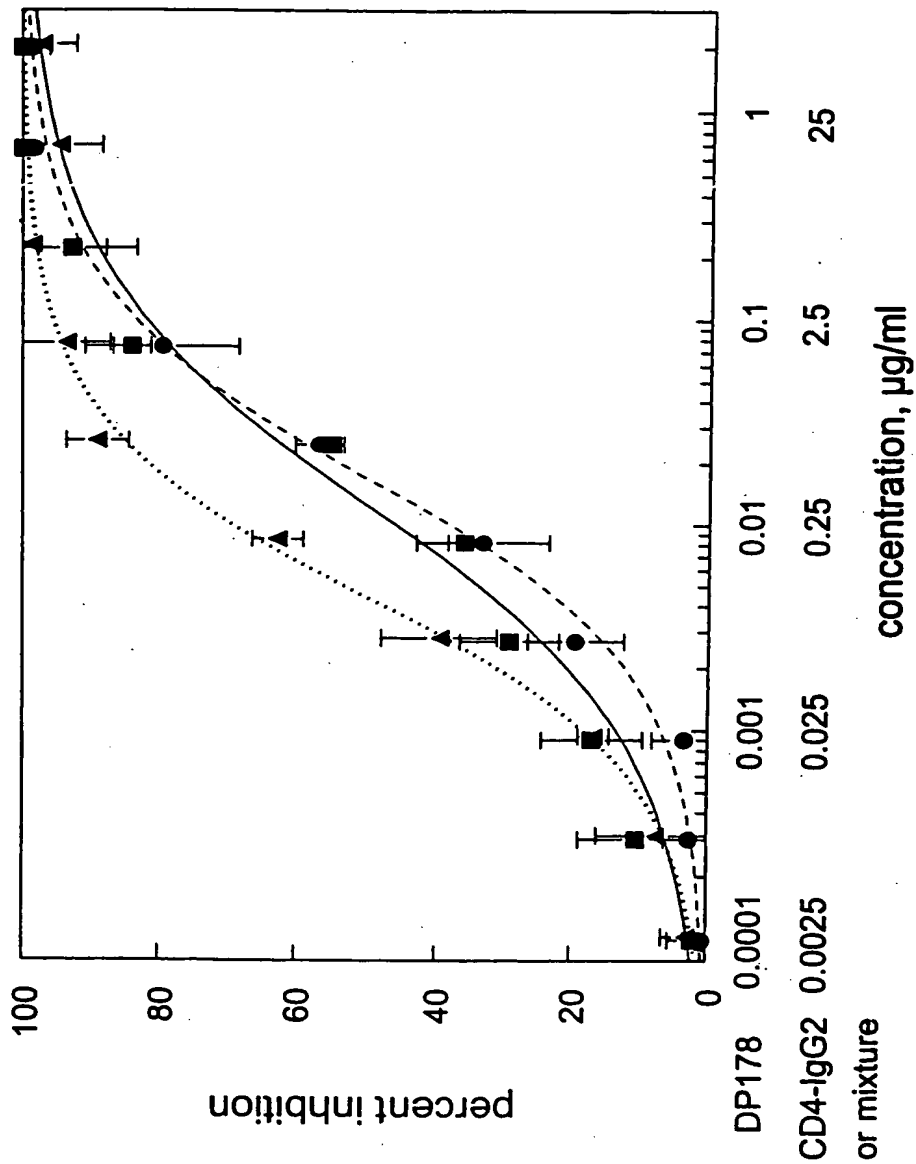


FIGURE 8



13/20

FIGURE 9

Percent Inhibition	Combination Index			
	CD4-IgG2:T-20 Mass Ratio			
	25:1 (low)	25:1 (high)	5:1	1:1
95	0.32	0.20	0.22	0.50
90	0.38	0.25	0.27	0.55
85	0.43	0.29	0.30	0.59
80	0.47	0.33	0.34	0.62
75	0.51	0.36	0.37	0.65
70	0.54	0.39	0.40	0.67
65	0.58	0.42	0.43	0.70
60	0.61	0.45	0.45	0.73
55	0.65	0.48	0.49	0.75
50	0.69	0.51	0.52	0.78

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FIGURE 10

Percent Inhibition	T-20			CD4-IgG2		
	Concentration, µg/ml		Dose Reduction	Concentration, µg/ml		Dose Reduction
	Alone	Combination		Alone	Combination	
99	1.1	0.17	6.6	130	4.3	29
95	0.21	0.044	4.9	19	1.10	17
90	0.10	0.024	4.2	7.8	0.59	13
70	0.025	0.0076	3.3	1.6	0.19	8.4
50	0.011	0.0039	2.8	0.60	0.095	6.3

FIGURE 11A

Percent Inhibition	Combination Index	PRO 542				PA12				T-20			
		Concentration, nM		Dose Reduction		Concentration, nM		Dose Reduction		Concentration, nM		Dose Reduction	
		Alone	Mix	Alone	Mix	Alone	Mix	Alone	Mix	Alone	Mix	Alone	Mix
95	0.41	10	2.1	4.8	730	2.8	260	94	19	4.9			
90	0.45	7.0	1.6	4.4	320	2.1	150	63	14	4.5			
70	0.47	4.1	0.92	4.5	72	1.2	60	30	8.1	3.7			
50	0.48	3.1	0.66	4.7	28	0.87	32	19	5.8	3.3			

PRO 542, PA12 and T-20 were used in an approximate 1:1:10 molar concentration ratio.

FIGURE 11B

Percent Inhibition	Combination Index	PRO 542				PRO 140				T-20	
		Concentration, nM		Dose Reduction		Concentration, nM		Dose Reduction		Concentration, nM	
		Alone	Mix	Alone	Mix	Alone	Mix	Alone	Mix	Alone	Mix
95	0.40	8.5	1.9	4.5	1.0	19	1.0	19	17	140	17
90	0.39	7.1	1.5	4.7	0.77	13	0.77	17	13	100	13
70	0.37	5.3	0.87	6.1	0.46	7.2	0.46	16	7.7	57	7.7
50	0.35	4.6	0.63	7.3	0.34	4.9	0.34	14	5.6	40	5.6

PRO 542, PRO 140 and T-20 were used in an approximate 2:1:20 molar concentration ratio.



FIGURE 11C

Percent Inhibition	Combination Index	PRO 542				PRO 140				T-20	
		Concentration, nM		Dose Reduction		Concentration, nM		Dose Reduction		Concentration, nM	
		Alone	Mix	Alone	Mix	Alone	Mix	Alone	Mix	Alone	Mix
95	0.24	61	2.5	24	11.9	0.72	17	156	22	7.1	
90	0.22	32	1.4	23	8.4	0.40	21	96	13	7.4	
70	0.19	9.8	0.50	20	4.5	0.14	32	40	4.5	8.9	
50	0.18	4.7	0.26	18	3.0	0.074	41	23	2.3	10	

PRO 542, PRO 140 and T-20 were used in an approximate 4:1:30 molar concentration ratio.

FIGURE 11D

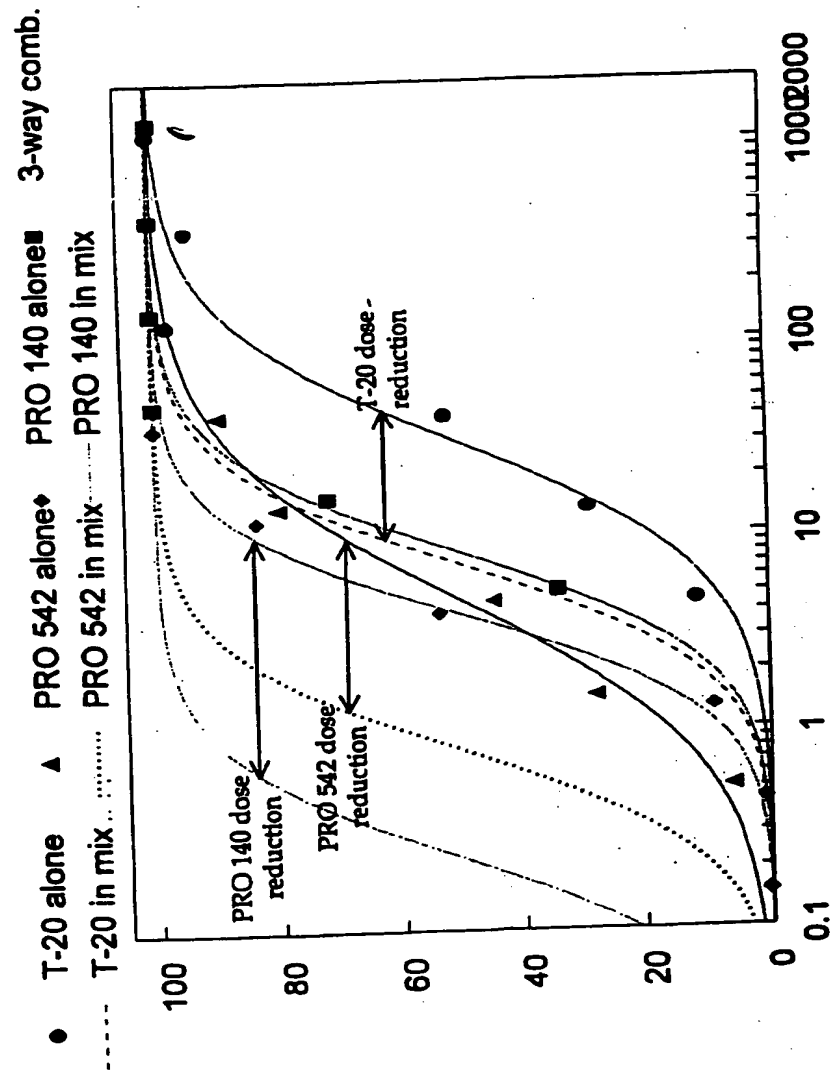
Percent Inhibition	Combination Index	PRO 140				T-20			
		Concentration, nM		Dose Reduction		Concentration, nM		Dose Reduction	
		Alone	Mix	Alone	Mix	Alone	Mix	Alone	Mix
95	0.56	12	1.8	6.7	156	55	2.8		
90	0.55	8.4	1.1	7.4	96	35	2.7		
70	0.55	4.5	0.51	8.8	40	16	2.5		
50	0.56	3.0	0.31	9.9	23	10	2.4		

PRO 140 and T-20 were used in an approximate 1:30 molar concentration ratio.

19/20

FIGURE 12

*Triple Combination Synergistically Blocks HIV-1 Entry (1)*



20/20

FIGURE 13

